PCN156

COMPARATIVE RESPONSIVENESS OF DIRECT AND MAPPED SF-6D PREFERENCE-BASED MEASURES IN COLORECTAL CANCER

Wong CKH[1], Mulhern B[2], Wan YF[1], Lam CLK[1]

[1]*The University of Hong Kong, Hong Kong Island, Hong Kong,* [2]*University of Sheffield, Sheffield, UK*

OBJECTIVES: This study examined the responsiveness of preference-based measures based on the anchor of self-reported change in general health condition of patients with colorectal cancer (CRC). **METHODS:** A baseline sample of 333 patients was recruited at the specialist outpatient clinic of academic teaching hospital in Hong Kong between September 2009 and July 2010, and was surveyed prospectively at 6-month follow-up. SF-6D preference-based indices were derived from the generic SF-6D measure ($SF\text{-}6D_{Direct}$), from the Short Form-12 Health Survey ($SF\text{-}6D_{SF\text{-}12}$) and also mapped from the condition-specific Functional Assessment of Cancer Therapy-Colorectal ($SF\text{-}6D_{FACT\text{-}C}$). The responsiveness of three measures was assessed using the internal responsiveness and external responsiveness. The 95% bias-corrected and accelerated bootstrapping confidence intervals were performed to compare the internal responsiveness statistics measured by standardized effect size, standardized response mean, and responsiveness statistic. External responsiveness was evaluated by receiver operating characteristic (ROC) curve analysis that examined the ability to detect score changes with global health condition changes or discriminate between the worsened and unchanged/improved groups. **RESULTS:** Over half of patients reported no change in global health condition based on the self-reported anchor, whilst 15.1% and 32.9% of patients rated better and worse in current health condition compared to baseline respectively. In worsened group, internal responsiveness was satisfactory for the $SF\text{-}6D_{Direct}$ and $SF\text{-}6D_{FACT\text{-}C}$ preference-based indices. The $SF\text{-}6D_{SF\text{-}12}$ and $SF\text{-}6D_{FACT\text{-}C}$ indices were significantly more responsive to detect positive changes than the $SF\text{-}6D_{Direct}$ index in improved group. The $SF\text{-}6D_{Direct}$ and $SF\text{-}6D_{FACT\text{-}C}$ indices were more externally responsive based on ROC curve. The $SF\text{-}6D_{FACT\text{-}C}$ index was generally more responsive to changes in health status compared with other indices. **CONCLUSIONS:** Direct SF-6D measure was more responsive than mapped preference-based measures in improved group but the direction was reversed in worsened group. Use of a preference-based index mapped from a condition-specific measure captures both negative and positive important changes in HRQOL score among CRC.

PCN157

QUALITY OF LIFE IN PATIENTS WITH METASTATIC COLORECTAL CANCER (MCRC): A UTILITIES STUDY IN THE UNITED KINGDOM AND THE NETHERLANDS

Stein D[1], Joulain F[2], Iqbal SU[3], Naoshy S[3], Muszbek N[4], Payne KA[1], Ferry DR[5]

[1]*Evidera, Dorval, QC, Canada,* [2]*Sanofi, Chilly-Mazarin, France,* [3]*Sanofi, Cambridge, MA, USA,* [4]*Evidera, London, UK,* [5]*The Dudley Group NHS Foundation Trust, Dudley, UK*

OBJECTIVES: To elicit utility values from EQ-5D for patients with various stages of mCRC. **METHODS:** An observational cross-sectional study consisting of one-time EQ-5D completion at enrollment was conducted in five hospitals in The Netherlands and the United Kingdom (UK). Patients were categorized into stable or progressed cohorts based on investigator assessment. Patients with mCRC were eligible if on second or subsequent lines of treatment or best supportive care [BSC], received prior oxaliplatin, no prior irinotecan, and had Eastern Cooperative Oncology Group (ECOG) performance status scores of 0-2 at second line initiation similar to the VELOUR trial. Chart data on patient demographics, clinical history, prior/current treatments, serious adverse events (SAEs) were collected. Average utilities were estimated; uni- and multivariate analyses were conducted. **RESULTS:** A total of 75 patients were enrolled, 42 patients stable on second line or third line following an AE on second line and 33 progressed patients. Mean age was 63 (standard deviation [SD]=10); 52% male. Most patients in the stable (98%) and progressed (88%) cohorts had ECOG scores of 0-1 at enrollment. 7% and 15% of patients in stable and progressed cohorts respectively had ongoing SAEs at enrollment. Mean utility scores were 0.741 (SD=0.230) and 0.731 (SD=0.292) for stable and progressed patients respectively. Higher proportions of patients reported increased anxiety/depression (36% vs. 12%) and fewer problems with daily activities post-progression (64% vs. 38%). 83% and 42% of patients in stable and progressed cohorts respectively, were on treatment at enrollment. **CONCLUSIONS:** While the majority of the stable cohort had good performance status and few SAEs ongoing at enrollment, utility values were not much higher compared to the progressed cohort. Higher values in the progressed cohort may be attributed to exclusion of patients in palliative care centers, radiological versus symptomatic disease progression and patients remaining on treatment, having few SAEs and good performance status at enrollment.

PCN158

UTILITY VALUES USED IN NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE) TECHNOLOGY APPRAISALS OF MEDICINES FOR 4 METASTATIC CANCERS

Burke MJ[1], Sidhu R[2], George E[2]

[1]*National Institute for Health and Care Excellence, Manchester, UK,* [2]*National Institute for Health and Care Excellence, London, UK*

OBJECTIVES: National Institute for Health and Care Excellence (NICE) considers the quality-adjusted life year (QALY) to be the most appropriate generic measure of health benefit that reflects both mortality and health-related quality of life effects. The QALY is the sum of a person's length of life in each health state multiplied by a quality-adjustment weight (that is, utility value) associated with that health state. Cost-effectiveness results are often sensitive to the choice of utility value, but relevant and comparable utility values are not always available leading to debate about the most appropriate utility values to include. The objective of the research was to review the health-related utility values used in economic models across NICE technology appraisal guidance for 4 metastatic cancers. **METHODS:** A cross-sectional review of manufacturer submissions and reports produced by independent academic groups was carried out to identify the health-related utility values used. Information relating to the methods used to elicit utility values that were selected for use in cost-effectiveness analyses were compared with methods specified by NICE as the reference case in its 2004 and 2008 Methods Guides. The review focused on guidance published before June 2013 for medicines treating metastatic breast cancer, metastatic colorectal cancer, metastatic hormone-refractory prostate cancer and metastatic non-small-cell lung cancer. Nineteen technology appraisals published between March 2002 and August 2012 met the inclusion criteria. **RESULTS:** Common themes or variations that exist between utility values selected by manufacturers and independent academic groups for each metastatic cancer and between the 4 metastatic cancers were analysed. The research also explored the methodological issues that were considered by the Appraisal Committee relating to the selection of utility values. **CONCLUSIONS:** Therefore, this research provides insight to the methodological considerations regarding incorporation of utility values that have informed health technology assessment decision-making in England for 4 metastatic cancers.

PCN159

PATIENTS' AND CAREGIVERS' PREFERENCES FOR BONE METASTASES (BM) TREATMENTS IN THE UNITED STATES

Qian Y[1], Mohamed AF[2], Hauber AB[2], Collins H[1], Hechmati G[3], Gatta F[3], Arellano J[1]

[1]*Amgen Inc., Thousand Oaks, CA, USA,* [2]*RTI Health Solutions, Research Triangle Park, NC, USA,* [3]*Amgen (Europe) GmbH, Zug, Switzerland*

OBJECTIVES: Patients with BM from solid tumors often experience skeletal-related events [SREs]; commonly defined as pathologic fracture, radiation or surgery to bone, and spinal cord compression. Several bone-targeted agents are approved for the prevention of SREs. This study evaluated US patients' and caregivers' preferences in relation to available treatment options in the US. **METHODS:** Adults with or adult caregivers of patients with a self-reported physician diagnosis of BM from a solid tumor completed a web-enabled discrete-choice experiment survey comprising a series of 10 choices between pairs of hypothetical medication profiles. Each profile included 6 medication attributes within a pre-defined range (primarily based on prescribing information and real-world practice): months until first SRE (10, 18 and 28 months); months until worsening of pain (3, 6, 10 months); annual risk of osteonecrosis of the jaw (ONJ; 0%, 1%, 5%); annual risk of renal impairment (0%, 4%, 10%); mode of administration (subcutaneous injection, 15-minute infusion, 120-minute infusion); and monthly out-of-pocket cost to patients ($25, $75, $150, $330). Choice questions were based on an experimental design with known statistical properties. The survey was pretested with 15 patients and 11 caregivers using open-ended interviews. A separate main-effects random parameters logit model was estimated. **RESULTS:** In total, 187 patients and 197 caregivers completed the survey. Among the attribute levels included, out-of-pocket cost to patients, risk of renal impairment, and months until first SRE were most important to both patients and caregivers. For those attributes, better outcomes were preferred to worse outcomes ($p<0.05$) except that risk of renal impairment between 4% and 10% was not significant for patients; costs between $25 and $75 were not significant for either group. **CONCLUSIONS:** When considering treatment choices for preventing skeletal complications associated with BM, patients and caregivers focused mainly on out-of-pocket cost to patients, avoiding renal impairment, and delaying SREs.

PCN160

CLINICAL OUTCOME ASSESSMENTS IN FDA ONCOLOGY LABELS SINCE 2010

Meyers OI[1], Foley K[2]

[1]*Truven Health Analytics, Cleveland, OH, USA,* [2]*Truven Health Analytics, Cambridge, MA, USA*

OBJECTIVES: In 2009, the FDA released Final Guidance on Patient-Reported Outcomes (PROs) and has stated that standards for PROs apply equally to Clinician and Observer Reported Outcomes (ClinROs, ObsROs; collectively, clinical outcome assessments - COAs). The objective was to survey labels for oncologic drugs approved in the three years since the "PRO Guidance" was finalized and to characterize any COAs in these labels. **METHODS:** CenterWatch maintains a list of FDA approved drugs following definitions established by the Tufts Center for the Study of Drug Development, including only drugs or NMEs newly approved by the FDA Center for Drug Evaluation and Research. From 2010 to the time of this review in 2013, 45 oncologic drugs were approved by the FDA. The FDA approved product labels of each of these drugs was reviewed and each was tabulated according to its inclusion of COAs. **RESULTS:** Few of the approved product labels reviewed included any reference to, much less data collected using PROs, ClinROs, or ObsROs. Several (e.g., carfilzomib) had clear statements to indicate that approval for the product was based on a predefined response rate rather than any "improvement in survival or symptoms." The notable exceptions are fentanyl sublingual tablets and spray and abiraterone, with PRO data on pain. **CONCLUSIONS:** There are several explanations for the low rate of COAs in oncology labels, especially that oncology trials tend to be unblinded. The FDA has stated that open label designs cannot support PRO claims. Yet there is still a heavy reliance on outcomes such as progression free and overall survival. Three labels were identified with PRO data on pain, two of which were specifically indicated for pain rather than tumor control. This review suggests there are opportunities for sponsors and the FDA to increase the degree to which the patient's voice is heard during the regulatory decision making process.

PCN161

SYSTEMATIC REVIEW OF PATIENT REPORTED OUTCOMES IN CHRONIC MYELOID LEUKEMIA

Aggarwal S, Segal J, Topaloglu H

Novel Health Strategies, Bethesda, MD, USA

OBJECTIVES: Patient reported outcomes (PRO) are becoming useful tools for collecting and generating evidence for new medical products to show improvements in health-related quality of life (HRQoL). Chronic myeloid leukemia (CML) is now a chronic disease in which HRQoL is becoming important. The objective of this study was to review, analyze, and understand trends in the PRO instruments used in patients with CML. **METHODS:** A systematic literature search for CML randomized controlled trials (RCTs) with PROs endpoints was undertaken for the databases Pubmed, Embase, Biosis, Google Scholar, and Cochrane. Data was collected for the study size, interven-

tions, year, PRO instrument, and results for PROs. Analysis was conducted to identify trends in commonly used PRO instruments and results were categorized as positive, neutral, or negative. **RESULTS:** Eight RCTs with a total of 3,342 patients were identified. In these studies, there were eight different PROs instruments identified: FACT-Leu, SF-36, FSI, PSQI, MSAS-SF, FACT-BRM, EQ-5D, and MDASI-CML. The most commonly used instruments were FACT-Leu (used in 1,336 patients) and FACT-BRM (used in 1,199 patients). Five studies reported positive results with improvement in quality of life (QoL) symptoms versus comparator treatments. Two studies reported results highlighting significant deterioration in QoL versus patients with no cancer. One study reported QoL in various types of CML and showed significant deterioration in patients with chronic phase CML versus those with acute and blast phase CML. Studies also identified two QoL domains, depression and fatigue, which matter most for patients with CML. **CONCLUSIONS:** Patients with CML have significant deterioration in their QoL. PRO instruments such as FACT-Leu and FACT-BRM can aid in generating evidence to show which therapies improve patient QoL.

PCN162

PATIENT REPORTED OUTCOMES IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Aggarwal S, Segal J, Kumar S
Novel Health Strategies, Bethesda, MD, USA

OBJECTIVES: Patient reported outcomes (PRO) are becoming useful tools for collecting and generating evidence for new medical products to show improvements in health-related quality of life (HRQoL). Castration-Resistant Prostate Cancer (CRPC) is a chronic disease with high importance for patient HRQoL. The objective of this study was to review, analyze, and understand trends in the PRO instruments used in patients with CRPC. **METHODS:** A systematic literature search for CRPC randomized controlled trials (RCTs) with PROs endpoints was undertaken for the databases Pubmed, Embase, Biosis, Google Scholar, and Cochrane. Data was collected for the study size, interventions, year, PRO instrument, and results for PROs. Analysis was conducted to identify trends in commonly used PRO instruments and categorize results as positive, neutral or negative. **RESULTS:** Ten RCTs with a total of 5,797 patients were identified. In these studies there were thirteen different PROs instruments were identified that were FACT-P, FACT-G, BPI-SF, EQC30, EQPR25, FLIC, SDS, SUF, PDA, IPDA, PROSQOLI, SF-36, and QOLM-P14. The most commonly used instrument were FACT-P (used in 4,297 patients) and EQC-30 (used in 1,091 patients). Six studies reported positive results with improvement in quality of life symptoms (QoL) versus comparator treatments. Fours studies reported results with deterioration in (QOL). Three studies reported improvement in pain scores. **CONCLUSIONS:** Patients with CRPC have relatively longer survival and hence QoL is an important consideration for these patients. PRO instruments such as FACT-P and EQC-30 have been commonly used to generate evidence to show which therapies improve patient QoL.

PCN163

ARE "DIZZY" AND "LIGHTHEADED" THE SAME CONCEPT OR SEPARATE CONCEPTS? CHALLENGES IN CONCEPTUAL EQUIVALENCE OF THESE TERMS IN 20 LANGUAGES

Eremenco S[1], Arnold BJ[2]
[1]*Evidera, Bethesda, MD, USA,* [2]*FACITtrans, Elmhurst, IL, USA*

OBJECTIVES: Feeling "dizzy" or "lightheaded" are common concepts in patient-reported outcome (PRO) instruments in a number of conditions. The Functional Assessment of Cancer Therapy – Anemia (FACT-An) subscale contains an item assessing "feeling dizzy (lightheaded)" as one concept while other instruments propose to assess the symptoms as two separate concepts or items. The purpose of this study was to translate and assess conceptual equivalence of this concept across 20 languages (21 countries). **METHODS:** The FACT-An was translated following the FACIT Translation methodology which is consistent with ISPOR guidelines for translation and cultural adaptation of PRO measures (Wild et al., 2005). The translation process for each language consisted of: 2 forward translations by native translators, reconciliation of the forward translations, 1 back-translation by an English-speaker fluent in the target language, 3 reviews by native translators or clinicians, final reconciliation by a native speaking linguist, and harmonization. Interviews were conducted among 456 native-speaking patients in 21 countries. Data were analyzed to assess linguistic and cultural validity of the FACT-An in each language and confirm conceptual equivalence. **RESULTS:** Mean age of the sample (N=456) was 55 years, (range 19-88) and 58% were male. During the translation phase, 12 of the 20 languages translated the concept of dizzy (lightheaded) using only one term, and the remaining 8 languages provided two terms. The rationale was that one word was used to describe this set of symptoms and it would be a complicated explanation to address the second term. The translations were well understood and considered relevant. **CONCLUSIONS:** The majority of languages in this study provided only one term for the concept of dizzy (lightheaded) indicating that it may be problematic to assess the concept as two separate symptoms in future questionnaires in other languages where this concept is not separated as it is in English.

PCN164

PRO CLAIMS IN JAPANESE ONCOLOGY PRODUCT LABELING

Crawford B
Adelphi Values, Tokyo, Japan

OBJECTIVES: There is a growing use of patient-reported outcomes (PRO) in the US and Europe but little is known about Asia. Oncology in particular is an area of growing interest. This study sought to review PRO labeling within oncology products over the last five years in Japan. **METHODS:** Oncology labels were identified by reviewing the Pharmaceutical and Medical Devices Agency (PMDA) postings of label changes for the past 5 years (2007-2012). For identified products with label changes, labels and Interview Forms (IF) were acquired and reviewed. The IF is used as a supplement to the label in Japan to provide additional data that will not fit within the package insert. Only PROs used for potential promotion were evaluated. Symptoms such as pain listed in the adverse events or safety sections were not included in this review. **RESULTS:** A total of 84 active ingredients had new indications or label changes. After removal of 25 duplicate ingredients (or updated again during this timeframe), 59 labels and IFs were identified and reviewed. No product labels contained PRO information. However, in contrast 20 (34%) IFs contained PRO information. 10 of these IFs only stated that "QOL" or "PRO" was assessed without details on the questionnaires or results. The EORTC (European Organisation for Research and Treatment of Cancer) and FACT (Functional Assessment of Cancer Therapy) were explicitly stated as measures in four and three IFs, respectively. There were also three pain assessments; two Visual Analog Scale assessments and one utilizing the Brief Pain Inventory – Short Form (BPI-SF). **CONCLUSIONS:** Although no oncology labels contained PRO information, the IFs contained PRO information. 1/3 of product information contained a mention of PROs which can be used in discussions with clinicians.

PCN165

CHANGES IN PATIENT-REPORTED OUTCOMES AMONG PEDIATRIC LEUKEMIA AND LYMPHOMA PATIENTS DURING THE FIRST 2-YEARS POST ALLOGENEIC STEM CELL TRANSPLANTATION (ALLOSCT)

Oberg JA[1], Morris E[2], Cairo M[2], Kelly KM[1]
[1]*Columbia University, New York, NY, USA,* [2]*New York Medical College, Valhalla, NY, USA*

OBJECTIVES: To explore changes in child-reported quality of life (QOL) of pediatric leukemia/lymphoma patients receiving alloSCT. **METHODS:** Hierarchical linear modeling was used to explore trends in select PedsQL 4.0 sub-scales and individual items of 43 children ≥5 years of age. QOL was assessed once pre-alloSCT and on days 100, 180, 365, and 730, post-alloSCT. **RESULTS:** Median age: 13.54 years, Range: 4.66-23.12 years; leukemia: 76.7%; lymphoma: 23.3%; reduced-toxicity conditioning (RTC)/myeloablative conditioning (MAC): 44%/56%; chronic graft-versus-host disease (cGVHD): 27.9%. Emotional and social functioning was stable pre-to-post-alloSCT and comparable to a normative pediatric sample ($p>.05$), whereas physical functioning was 19 points lower pre-alloSCT ($M=67.42$; $p<.01$; $ES=1.26$SD) with improved scores approaching norms by Day +730. 51-65% of children at baseline reported difficulties with sports/exercise, strength, pain, and fatigue. Significant improvements from baseline ($M=51.41$) were observed in sports/exercise at a rate of 1.06 points-per-month (ppm)/12.90 points-per-year (ppy) ($t=2.57$; $p=.01$) and strength ($M=47.47$; $t=2.05$; $p=.04$) at a rate of 0.84 ppm (10.21ppy). Recipients of RTC significantly improved at a rate of 14.04ppy (slope=1.16; $t=2.41$; $p=.02$) compared to children who received MAC (-4.01ppy; slope=-0.33). Similarly gains in strength were significantly better for the RTC group (12.94ppy; slope=1.06; $t=2.25$; $p=.02$) than the MAC group (-10.62ppy; slope=-0.83). Levels of pain ($M=64.82$; slope= 0.05ppm; $t=0.15$; $p=.88$) and fatigue ($M=58.01$; slope=0.39ppm; $t=1.14$; $p=.26$) remained unchanged irrespective of conditioning regimen. Emotional functioning of children ages 8-12 significantly improved from baseline ($M=70.18$; slope=1.78ppm; $t=2.89$; $p=.01$), whereas children ≥13 significantly declined post-alloSCT ($M=72.61$; slope=-1.34ppm; $t=-2.64$; $p=.01$). Presence of cGVHD did not significantly affect outcomes scores. **CONCLUSIONS:** Improvements in exercise and strength were seen with RTC regimens whereas pain and fatigue remained unchanged independent of conditioning regimen. Older children may have more emotional difficulties post-alloSCT. These results highlight the importance of including QOL to monitor patients and further define outcomes for this population.

PCN166

QUALITY OF LIFE IN PATIENTS WITH OSTOMY IN POLAND: MULTICENTRE CROSS-SECTIONAL STUDY USING WHOQOL-BREF QUESTIONNAIRE

Golicki D[1], Styczen P[2], Szczepkowski M[3]
[1]*Department of Experimental and Clinical Pharmacology, Medical University of Warsaw, Warsaw, Poland,* [2]*Gabinet Lekarski, Konopiska, Poland,* [3]*Faculty of Rehabilitation, Jozef Pilsudski University of Physical Education in Warsaw, Warsaw, Poland*

OBJECTIVES: To assess quality of life of Polish patients with a stoma using validated generic questionnaire. **METHODS:** Adult patients with colostomy, ileostomy or urostomy performed in Poland between July 2009 and December 2010 were included. Patients completed satisfaction survey at the discharge from the hospital, and The World Health Organization Quality of Life-BREF (WHOQOL-BREF) generic questionnaire at 3 months after surgery. **RESULTS:** The study involved 1519 patients (71.5%, 16.8%, 11.7% with colostomy, ileostomy and urostomy, respectively). The studied population was highly diversified in terms of: pain and discomfort, dependence on medical treatment and acceptance of physical appearance. 57% of patients with a stoma defined their quality of life as good or very good (mean 3.54 points; range: 1 to 5; SD 0.73). The subjects were characterized by low quality of life assessment in the physical health and psychological domains (53.5 and 60.0 pts.) and by high evaluation in the environment and social relationships domains (69.6 and 70.2 pts.). Respondents highly assessed: the level of social support, home environment, physical environment, personal relationships. Low assessment was related to: sexual activity, ability to work, dependence on medical treatment, financial resources, satisfaction with health. **CONCLUSIONS:** This is the first Polish study on the quality of life of patients with a stoma, based on validated generic questionnaire. The results should help improve standards of care for patients with a stoma.

PCN167

INFLUENCE OF ANXIETY AND DEPRESSION ON 1-YEAR HEALTH RELATED QUALITY OF LIFE IN COLORECTAL CANCER PATIENTS

Escobar A[1], Billbao A[1], Trancho Z[1], Quintana J[2], Sarasqueta C[3], Baré M[4]
[1]*Basurto University Hospital (Osakidetza).Red de Investigación en Servicios Sanitarios y Enfermedades Crónicas (REDISSEC)., Bilbao, Spain,* [2]*Galdakao-Usansolo Hospital (Osakidetza). Red de Investigación en Servicios Sanitarios y Enfermedades Crónicas (REDISSEC)., Galdakao-Usansolo, Spain,* [3]*Donostia Universitary Hospital. Red de Investigación en Servicios Sanitarios y Enfermedades Crónicas (REDISSEC), Donostia, Spain,* [4]*Hospital Parc Tauli. Red de Investigación en Servicios Sanitarios y Enfermedades Crónicas (REDISSEC), Sabadell, Spain*

OBJECTIVES: To assess the impact of anxiety and depression measured by Hospital Anxiety and Depression Scale (HADS) on 1-year HRQoL measured by EuroQol-3L (EQ-5D) and EORTC-QLQ-C30 on patients with colorectal cancer. This aspect of continuity